HERU
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ECONOMIC EVALUATION OF URINARY BIOMARKERS AND CYSTOSCOPY WITH PHOTODYNAMIC DIAGNOSIS AND FOR DETECTION AND FOLLOW-UP OF BLADDER CANCER

Background

Bladder cancer is the fifth most common cancer in the UK, affecting more than 10,000 people each year, even after treatment these people have a risk of recurrent disease. The best way to diagnose patients with bladder cancer and follow them up after treatment is unclear. The ideal test for diagnosis and follow-up would be non-invasive, very accurate, inexpensive, easy to perform and would provide reproducible results. Many of the existing tests meet some of these criteria but it is unclear if any, used either alone or in combination, are cost-effective for the detection and follow-up of bladder cancer. In this study we considered the following tests used to diagnose and follow-up people with bladder cancer:

- Photodynamic cystoscopy (PDD) (an invasive test requiring a local or general anaesthetic)
- Rigid white light cystoscopy (WLC) (an invasive test requiring a local or general anaesthetic)
- Flexible cystoscopy (an invasive test requiring a local anaesthetic)
- Urine cytology (a non-invasive test requiring a urine sample)
- Urinary biomarkers (fluorescence in situ hybridisation [FISH], ImmunoCyt, nuclear matrix protein 22 [NMP22]) (non-invasive tests requiring a urine sample)

KEY MESSAGES

1. Bladder cancer is the fifth most common cancer in the UK, affecting more than 10,000 people each year.
2. Using non-invasive biomarkers and/or photodynamic cystoscopy to diagnose and follow-up patients with bladder cancer can provide additional benefits but are more costly.
3. The incremental cost per life-year is below typical thresholds, £20-£30,000 but a judgement is required as to whether the extra costs are worth the benefits.

CHIEF SCIENTIST OFFICE
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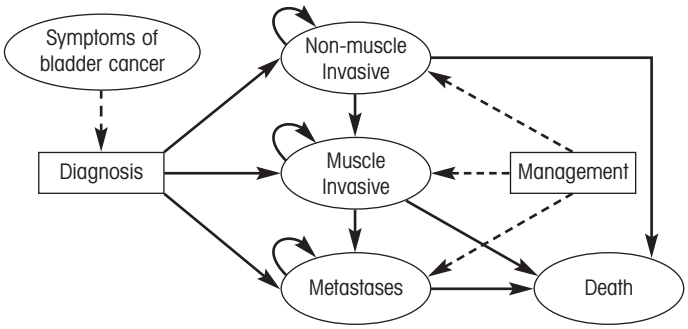
Method

Table 1 summarises the potential strategies considered in the model. These options were based on advice from clinical experts of those that are currently in use or those that can potentially be used. Strategies 1 to 6 consider the use of a single test for initial diagnosis. Strategies 7 to 16 represent alternative situations where two or more tests are used in the initial diagnosis. Across all strategies the choice of second level diagnostic test varied between WLC and PDD. The strategies also differ in terms of the tests used for follow-up surveillance. In the study we have assumed that a single test is used for initial surveillance with any positives confirmed by WLC.

The economic model described what happens to an individual from their initial presentation with suspected bladder cancer, through diagnosis and treatment over a 20-year time horizon. Figure 1 shows a simplified version of the model. Within this model, people with suspected bladder cancer receive tests and investigations to diagnose bladder cancer. Subsequent management depends upon the findings of these tests and the nature of bladder cancer detected. Over time an individual may die either as a result of bladder cancer or other causes.

Figure 1: Model Structure



The data to populate the model came from several sources. The probabilities of the sensitivity and specificity of diagnostic tests and risk classification were derived from the systematic reviews. Quality of life and cost data were all identified from published sources. Assumptions based on discussions with clinical experts were made where data were not readily available.

Table 1: Diagnostic Strategies

Strategy	Primary diagnosis					Follow-up surveillance			
	Initial test			Second test		Initial test			Second test
	CSC	CTL	BM	WLC	PDD	CSC	CTL	BM	WLC
1	✓			✓		✓			✓
2	✓				✓	✓			✓
3		✓		✓			✓		✓
4		✓			✓		✓		✓
5			✓	✓				✓	✓
6			✓		✓			✓	✓
7	✓	✓		✓		✓			✓
8	✓	✓			✓	✓			✓
9	✓	✓		✓			✓		✓
10	✓	✓			✓		✓		✓
11	✓		✓	✓		✓			✓
12	✓		✓		✓	✓			✓
13	✓		✓	✓				✓	✓
14	✓		✓		✓			✓	✓
15	✓	✓	✓	✓		✓			
16	✓	✓	✓		✓	✓			

CSC: flexible cystoscopy; CTL: cytology; BM: biomarker; WLC: white light cystoscopy; PDD photodynamic diagnosis.

Results

Strategies involving PDD were likely to detect more true positive cases and result in longer survival (measured in life-years) but be more costly than other strategies. The strategy involving "Flexible cystoscopy and ImmunoCyt followed by PDD for initial diagnosis and flexible cystoscopy followed by white light cystoscopy for follow-up surveillence," was the most effective (15.23 life years) strategy but also the most costly. Cytology followed by WLC in initial diagnosis and follow-up was the least effective (15.13 life years) and least costly. Strategies involving PDD were more likely to be cost-effective than strategies involving WLC.

Table 2 describes the results of the six strategies which were most likely to be cost-effective.

Sensitivity analysis

A sensitivity analysis was conducted to explore the uncertainty surrounding the data used to generate the result presented in Table 2. In Figure 2 none of the strategies were likely to be cost-effective more than 50% of the time except for strategy (1) [CTL_WLC (CTL-WLC)] when society is willing to pay relatively little for an additional life year. Nevertheless, three strategies involving the use of a biomarker each had a 20% chance of being cost-effective.

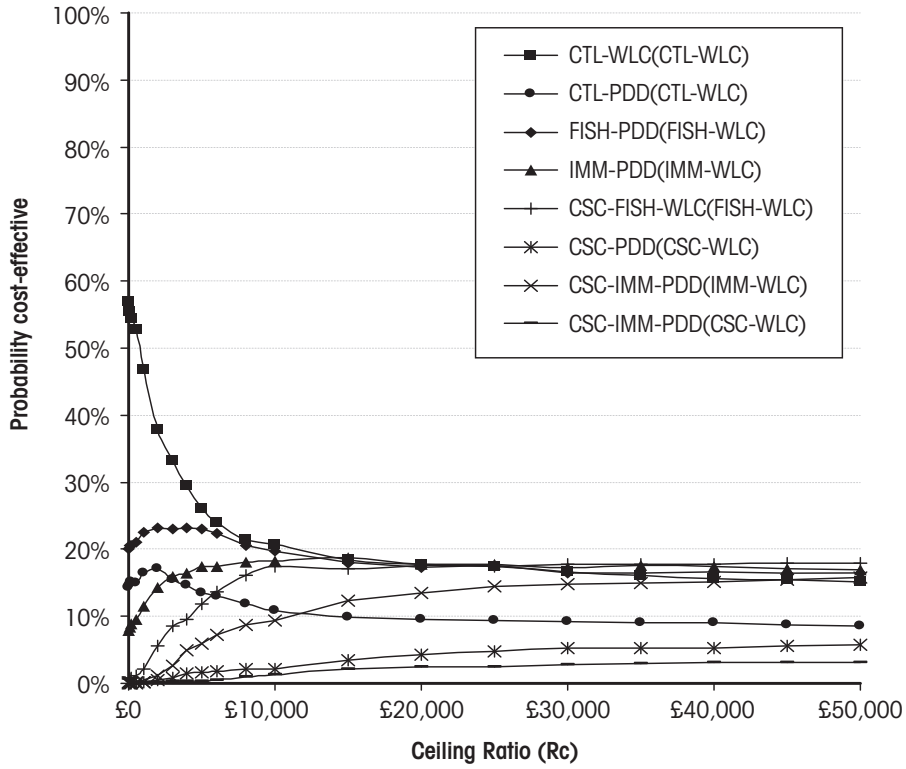
Another important area of uncertainty was the chance that someone presenting with symptoms actually had bladder cancer (set as 1 in 20 in the base case). When the risk was 1 in 100 the least costly (and least effective strategy) cytology followed by WLC for both diagnosis and follow-up was cost-effective.

Table 2: Results of the deterministic model for 20 year time horizon (per life-year) excluding dominated and extendedly dominated options

Strategy number	Strategy*	Cost	Incremental cost	Life years	Incremental years	ICER
1	CTL_WLC (CTL_WLC)	£1043		11.59		
2	CTL_PDD (CTL_WLC)	£1094	£51	11.6	0.01	£3423
3	FISH_PDD (FISH_WLC)	£1235	£141	11.64	0.04	£3806
8	IMM_PDD (IMM_WLC)	£1458	£223	11.65	0.01	£28864
16	CSC_FISH_PDD (FISH_WLC)	£2005	£547	11.66	0.01	£60284
26	CSC_IMM_PDD (CSC_WLC)	£2370	£365	11.66	<0.01	£270375

*Initial strategy (follow-up strategy)

Figure 2 Cost-effectiveness acceptability curves determined by society's willingness to pay for a life year for the eight strategies



Conclusions

Based on currently available data and taking into account the assumptions made in the model, the strategy of flexible cystoscopy and ImmunoCyt followed by PDD in initial diagnosis and flexible cystoscopy followed by WLC used for longer term surveillance is likely to be the most costly and the most effective (£2370 per patient and 11.66 life years). The strategy of cytology followed by WLC in initial diagnosis and follow-up is likely to be the least costly (£1043 per patient) and least effective in terms of life years (11.59) per patient. Which strategy is most cost-effective depends however on how much society would be willing to pay to obtain an additional life year.

For further details about this study see: Mowatt, G., Zhu, Z., Kilonzo, M., Boachie, C., Fraser, C., Griffiths, T.R.L., N'Dow, J., Nabi, G., Cook, J. and Vale, L. Systematic review of the clinical and cost-effectiveness of photodynamic diagnosis and urine biomarkers (FISH, ImmunoCyt, NMP22) and cytology for the detection and follow-up of bladder cancer. Health Technology Assessment 2010 Vol. 14 No. 4.

This briefing paper describes work conducted by the Assessment of Technologies Theme for the NIHR Health Technology Assessment Programme. Further information about this topic may be obtained by contacting Mary Kilonzo at HERU, University of Aberdeen, Foresterhill, Aberdeen AB25 2ZD (Tel: 01224 559106); Fax: (01224 550926); e mail m.kilonzo@abdn.ac.uk. For general information about HERU please contact Anne Bews at the below address or visit our Web site at http://www.abdn.ac.uk/heru.

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